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TO: Tamthom Truong
Location: REM-5C18
Art Unit: 1624
Wednesday, December 21, 2005

Case Serial Number: 10/776876

From: Mary Hale
Location: Biotech/Chem Library
Rem 1D86
Phone: 2-2507

Mary.Hale@uspto.gov

Search Notes

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( ) TC 2900 ( ) TC 3600 ( ) TC 3700 ( ) Law Lib ( ) Other

Your Contact Information:
* indicates mandatory information.

Your Name: Tamthom N. Truong
*Email Address: tamthom.ngo@uspto.gov
(e.g., Susan.Smith@uspto.gov)
*Employee No.: 74142
*Art Unit/Org.: 1624
*Office Location: REM 5B19
*Phone No.: x 20676
Mailbox No.: REM 5C18

DEC 13 2005 (1624)

***Case serial number:** 10/ 776,876
If not related to a patent application, please enter NA here.

13:29
1324
5min
$245.68

Class / Subclass(es) 514/269; 544/310, 311

Earliest Priority Filing Date: 05-01-1999

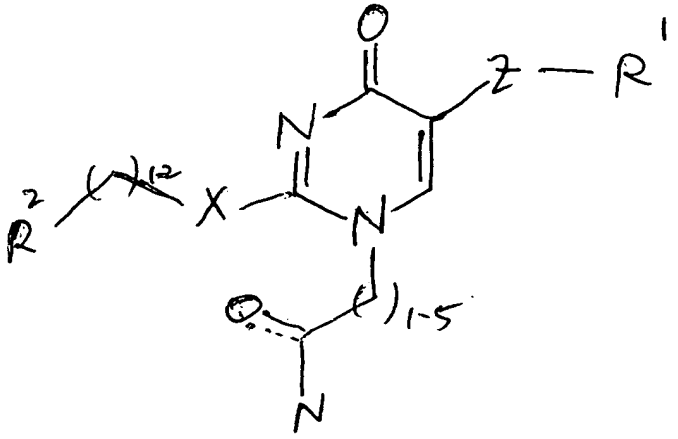
Format preferred for results:
☑ Paper ☐ Diskette ☐ E-mail

Query attached

Provide detailed information on your search topic:

- In your own words, describe in detail the concepts or subjects you want us to se
- Include synonyms, keywords, and acronyms. Define terms that have special me
- *For Chemical Structure Searches Only*
  Include the elected species or structures, keywords, synonyms, acronyms, and
- *For Sequence Searches Only*
  Include all pertinent information (parent, child, divisional, or issued patent numb
  serial number.
- *For Foreign Patent Family Searches Only*
  Include the country name and patent number.

10/776,876 Query



R^1 = aryl or heteroaryl group; (opt. sub.)

R^2 = (opt. sub.) aryl or heteroaryl group;

X = -O- or -S-;

Z = $CR^{13}R^{14}$

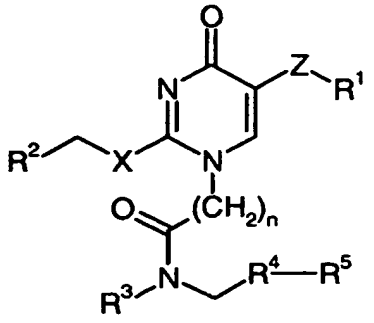
R^{13} + R^{14} = each is H, C_{1-5} alkyl.

See also attached claims 1 + 14 (species).

Serial No.: 10/776,876
Group Art Unit No.: 1624

Amendments to the Claims:

1. (Currently amended) A compound of formula (I):



(I)

in which:

R^1 is an aryl or heteroaryl group, optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from $C_{(1-18)}$alkyl, $C_{(1-18)}$alkoxy, $C_{(1-18)}$alkylthio, aryl$C_{(1-18)}$alkoxy, hydroxy, halogen, CN, COR^6, carboxy, $COOR^6$, $CONR^9R^{10}$, NR^6COR^7, $SO_2NR^9R^{10}$, $NR^6SO_2R^7$, NR^9R^{10}, mono to perfluoro-$C_{(1-4)}$alkyl and mono to perfluoro-$C_{(1-4)}$alkoxy, oxo, ~~or, as a single substituent, optionally in combination with a further substituent as hereinbefore defined,~~ CH_2COOH or a salt thereof, CH_2COOR^8, $CH_2CONR^9R^{10}$, CH_2CN, $(CH_2)_mNR^9R^{10}$, $(CH_2)_mOH$ or $(CH_2)_mOR^6$ where m is an integer from 1 to 3;

R^2 is an aryl or heteroaryl group, optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from $C_{(1-18)}$alkyl, $C_{(1-18)}$alkoxy, $C_{(1-18)}$alkylthio, aryl$C_{(1-18)}$alkoxy, hydroxy, halogen, CN, COR^6, carboxy, $COOR^6$, $CONR^9R^{10}$, NR^6COR^7, $SO_2NR^9R^{10}$, $NR^6SO_2R^7$, NR^9R^{10}, mono to perfluoro-$C_{(1-4)}$alkyl, mono to perfluoro-$C_{(1-4)}$alkoxy, and aryl$C_{(1-4)}$alkyl;

R^3 is hydrogen or $C_{(1-4)}$alkyl which may be unsubstituted or substituted by hydroxy, OR^6, COR^6, carboxy, $COOR^6$, $CONR^9R^{10}$, NR^9R^{10}, mono- or di-(hydroxy$C_{(1-6)}$alkyl)amino or N-hydroxy$C_{(1-6)}$alkyl-N-$C_{(1-6)}$alkyl amino;

R^4 is an aryl or a heteroaryl ring optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from $C_{(1-18)}$alkyl, $C_{(1-18)}$alkoxy, $C_{(1-18)}$alkylthio, aryl$C_{(1-18)}$alkoxy, hydroxy, halogen, CN, COR^6, carboxy, $COOR^6$, $CONR^9R^{10}$, NR^6COR^7, $SO_2NR^9R^{10}$, $NR^6SO_2R^7$, NR^9R^{10}, mono to perfluoro-$C_{(1-4)}$alkyl and mono to perfluoro-$C_{(1-4)}$alkoxy;

R^5 is an aryl ring which is further optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from $C_{(1-18)}$alkyl, $C_{(1-18)}$alkoxy, $C_{(1-18)}$alkylthio, aryl$C_{(1-18)}$alkoxy, hydroxy, halogen, CN, COR^6, carboxy, $COOR^6$, $CONR^9R^{10}$, NR^6COR^7, $SO_2NR^9R^{10}$, $NR^6SO_2R^7$, NR^9R^{10}, mono to perfluoro-$C_{(1-4)}$alkyl and mono to perfluoro-$C_{(1-4)}$alkoxy;

R^6 and R^7 are independently hydrogen or $C_{(1-20)}$alkyl, for instance $C_{(1-4)}$alkyl (e.g. methyl or ethyl);

R^8 is $C_{(1-4)}$alkyl or a pharmaceutically acceptable *in vivo* hydrolysable ester group;

R^9 and R^{10} which may be the same or different is each selected from hydrogen, $C_{(1-12)}$alkyl, CH_2R^{11}, $CHR^{12}CO_2H$ or a salt thereof, or R^9 and R^{10} together with the nitrogen to which they are attached form a 4- to 7-, preferably 5- to 7-, membered ring optionally containing one or more further heteroatoms selected from oxygen, nitrogen and sulphur, and optionally substituted by one or two substituents selected from hydroxy, oxo, $C_{(1-4)}$alkyl, $C_{(1-4)}$alkylCO, or aryl, ~~e.g. phenyl, or aralkyl, e.g benzyl, for instance morpholine or piperazine~~;

R^{11} is COOH or a salt thereof, $COOR^8$, $CONR^6R^7$, CN, CH_2OH or CH_2OR^6;

R^{12} is an amino acid side chain ~~such as CH_2OH from serine~~;

n is an integer from 1 to 4, preferably 1 or 3;

X is O or S; and

Z is $CR^{13}R^{14}$ where R^{13} and R^{14} are each hydrogen or $C_{(1-4)}$alkyl, or R^{13} and R^{14} together with the intervening carbon atom form a $C_{(3-6)}$cycloalkyl ring.

~~2. (original) A compound of formula (I) as claimed in claim 1 in which Z is~~ CH_2.

3. (Previously amended) ~~A compound of formula (I) as claimed in claim 1 in which~~ R^1 is an aryl group selected from phenyl and naphthyl or a heteroaryl group which comprises a 5- or 6- membered, monocyclic heteroaryl group comprising 1 or 2 nitrogen heteroatoms.

11. (Previously amended) A compound of formula (I) as claimed in claim 1 in which R^5 is phenyl optionally substituted by halogen, trifluoromethyl, or trifluoromethoxy.

12. (Previously amended) A compound of formula (I) as claimed in claim 10 in which R^4 and R^5 together form a 4-(phenyl)phenyl substituent in which the remote phenyl ring may be optionally substituted by halogen or trifluoromethyl.

13. (Deleted).

14. (Previously amended) A compound of formula (I) as claimed in claim 1selected from the group consisting of:

1-(N-methyl-N-(4-(4-chlorophenyl)benzyl)aminocarbonylmethyl)-2-(4-fluorobenzyl)thio-5-(1-methylpyrazol-4-ylmethyl)pyrimidin-4-one;

1-(N-methyl-N-(4-(4-trifluoromethylphenyl)benzyl)aminocarbonylmethyl)-2-(4-fluorobenzyl)thio-5-(1-methylpyrazol-4-ylmethyl)pyrimidin-4-one;

1-(N-(2-dimethylaminoethyl)-N-(4-(4-chlorophenyl)benzyl)aminocarbonylmethyl)-2-(4-fluorobenzyl)thio-5-(1-methylpyrazol-4-ylmethyl)pyrimidin-4-one;

1-(N-methyl-N-(4-(4-chlorophenyl)benzyl)aminocarbonylmethyl)-2-(4-fluorobenzyl)thio-5-(2-(4-morpholino)pyrimid-5-ylmethyl)pyrimidin-4-one;

1-(N-(2-(dimethylamino)ethyl)-N-(4-(4-trifluoromethylphenyl)benzyl)amino-carbonylmethyl)-2-(4-fluorobenzyl)thio-5-(1-methyl-4-pyrazolylmethyl)pyrimidin-4-one;

1-(N-(2-(diethylamino)ethyl)-N-(4-(4-chlorophenyl)benzyl)aminocarbonylmethyl)-2-(4-fluorobenzyl)thio-5-(1-methyl-4-pyrazolylmethyl)pyrimidin-4-one;

1-(N-(2-(diethylamino)ethyl)-N-(2-(4-trifluoromethylphenyl)pyrid-5-ylmethyl)-aminocarbonylmethyl)-2-(4-fluorobenzyl)thio-5-(1-methyl-4-pyrazolylmethyl)pyrimidin-4-one;

1-(N-(2-(1-piperidino)ethyl)-N-(4-(4-trifluoromethylphenyl)benzyl)aminocarbonylmethyl)-2-(4-fluorobenzyl)thio-5-(1-methyl-4-pyrazolylmethyl)pyrimidin-4-one bitartrate;

1-(N-(carboxymethyl)-N-(4-(4-trifluoromethylphenyl)benzyl)aminocarbonylmethyl)-2-(4-fluorobenzyl)thio-5-(1-methyl-4-pyrazolylmethyl)pyrimidin-4-one sodium salt; or

;

a pharmaceutically acceptable salt thereof.

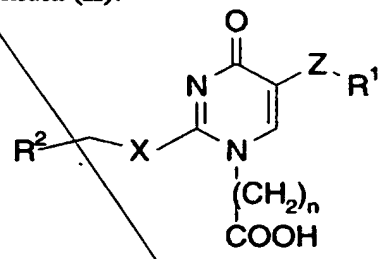
15. (Previously amended) A pharmaceutical composition comprising a compound of formula (I) as claimed in claim 14 and a pharmaceutically acceptable carrier.

16. – 18 (Deleted).

19. (original) A method of treating atherosclerosis which method comprises administering to a patient in need thereof an effective amount of a compound of formula (I) as claimed in claim 1 and a statin.

20. (original) A process for preparing a compound of formula (I) as defined in claim 1 which process comprises:

(a) reacting a compound of formula (II):



(II)

in which X, Y, Z, R^1 and R^2 are as defined in claim 1,

with a compound of formula (III):

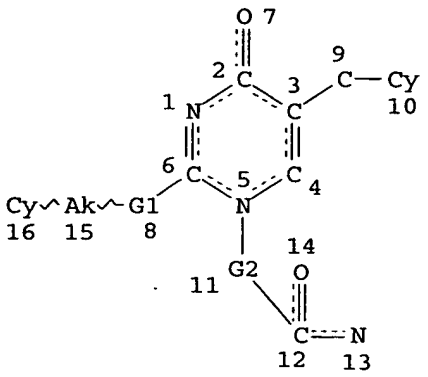
$$R^5\text{-}R^4\text{-}CH_2NHR^3$$

(III)

in which R^3, R^4 and R^5 are as defined in claim 1; under amide forming conditions;

Truong
10/776876

=> d l3 que stat;fil caplus;s l3
L1 STR



VAR G1=O/S
REP G2=(1-5) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
L3 191 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 5052 ITERATIONS 191 ANSWERS
SEARCH TIME: 00.00.01

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Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

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L4          11 L3

=> s l4 and pd<may 1999
      19822999 PD<MAY 1999
                 (PD<19990500)
L5           0 L4 AND PD<MAY 1999

=> d l4 1-11 ibib abs fhitstr

L4   ANSWER 1 OF 11  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:1177949  CAPLUS
DOCUMENT NUMBER:          143:434728
TITLE:                    Methods for detecting Lp-PLA2 activity and inhibition
                          of Lp-PLA2 activity
INVENTOR(S):              Shou, Yaping; Siu, Yin-Fai; Walker, George T.
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 26 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     US 2005244913         A1    20051103    US 2005-106239          20050414
     WO 2005113797         A2    20051201    WO 2005-US12948         20050414
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
             SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
             ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                       US 2004-563078P     P  20040416
AB   The invention discloses methods for determining the activity of Lp-PLA2 (PAF
     acetylhydrolase) in at least one sample from an animal.  The invention
     also discloses methods for determining the inhibition of Lp-PLA2 activity in
     samples from animals that are administered an Lp-PLA2 inhibitor.
IT   304694-39-1
     RL: PAC (Pharmacological activity); BIOL (Biological study)
        (methods for detecting Lp-PLA2 activity and inhibition of Lp-PLA2
        activity)
RN   304694-39-1  CAPLUS
CN   1(4H)-Pyrimidineacetamide, N-[2-(diethylamino)ethyl]-2-[[(4-
     fluorophenyl)methyl]thio]-5-[(1-methyl-1H-pyrazol-4-yl)methyl]-4-oxo-N-
     [[4'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]methyl]- (9CI)  (CA INDEX NAME)
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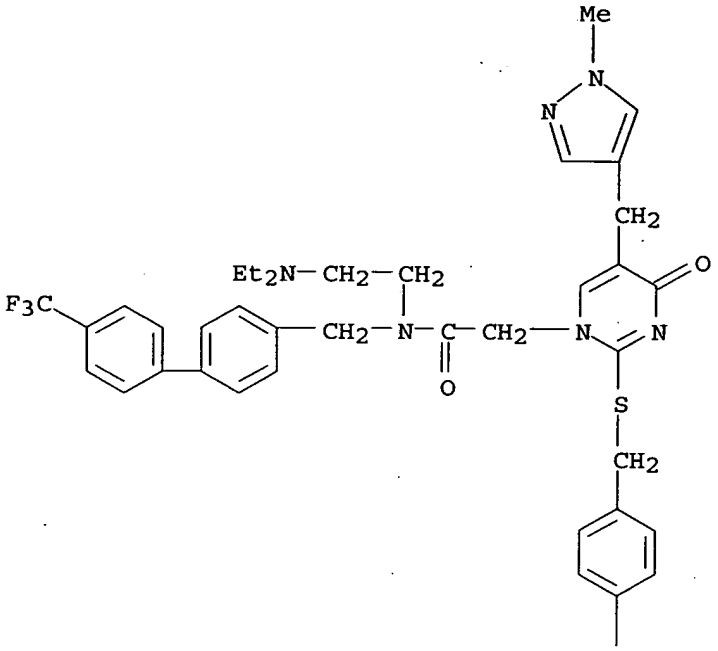
PAGE 1-A



PAGE 2-A

L4 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:215748 CAPLUS
DOCUMENT NUMBER: 139:78433
TITLE: The identification of clinical candidate SB-480848: a potent inhibitor of lipoprotein-associated phospholipase A2
AUTHOR(S): Blackie, Josie A.; Bloomer, Jackie C.; Brown, Murray J. B.; Cheng, Hung-Yuan; Hammond, Beverley; Hickey, Deirdre M. B.; Ife, Robert J.; Leach, Colin A.; Lewis, V. Ann; Macphee, Colin H.; Milliner, Kevin J.; Moores, Kitty E.; Pinto, Ivan L.; Smith, Stephen A.; Stansfield, Ian G.; Stanway, Steven J.; Taylor, Maxine A.; Theobald, Colin J.
CORPORATE SOURCE: Medicines Research Centre, GlaxoSmithKline, Stevenage, SG1 2NY, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(6), 1067-1070
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:78433

AB Modification of the pyrimidone 5-substituent in clin. candidate SB-435495

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

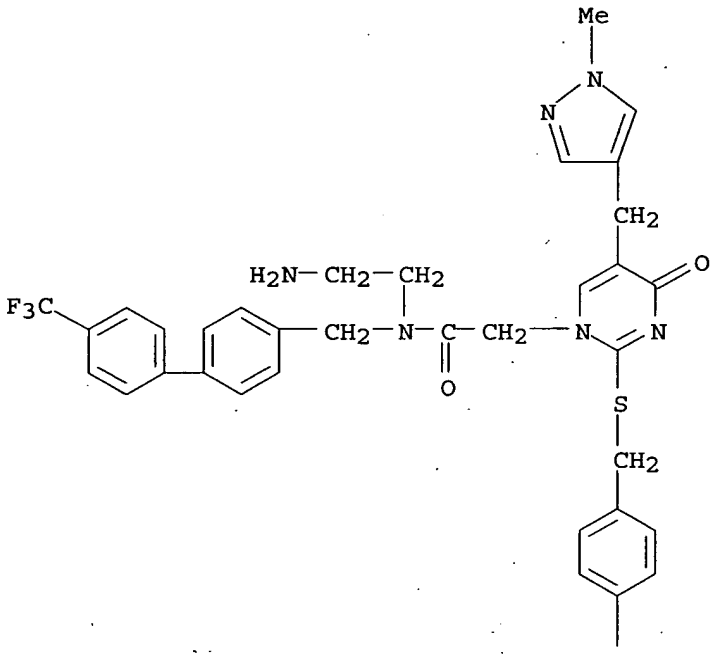
has given a series of inhibitors of recombinant lipoprotein-associated phospholipase A2 with sub-nanomolar potency. Cyclopentyl fused derivative 21, SB-480848, showed an enhanced in vitro and in vivo profile vs. SB-435495 and has been selected for progression to man.

IT **552857-42-8P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(design and structure activity of lipoprotein-associated phospholipase A2 inhibitor SB-480848)

RN 552857-42-8 CAPLUS

CN 1(4H)-Pyrimidineacetamide, N-(2-aminoethyl)-2-[[(4-fluorophenyl)methyl]thio]-5-[(1-methyl-1H-pyrazol-4-yl)methyl]-4-oxo-N-[[4'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:154252 CAPLUS
DOCUMENT NUMBER: 138:205073
TITLE: Preparation of 2,5-substituted 1-(aminocarbonylalkyl)-pyrimidin-4-ones with Lp-PLA2 inhibitory activity for the treatment of atherosclerosis

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

INVENTOR(S): Elliott, Richard Leonard; Leach, Colin Andrew; Smith, Stephen Allan
PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

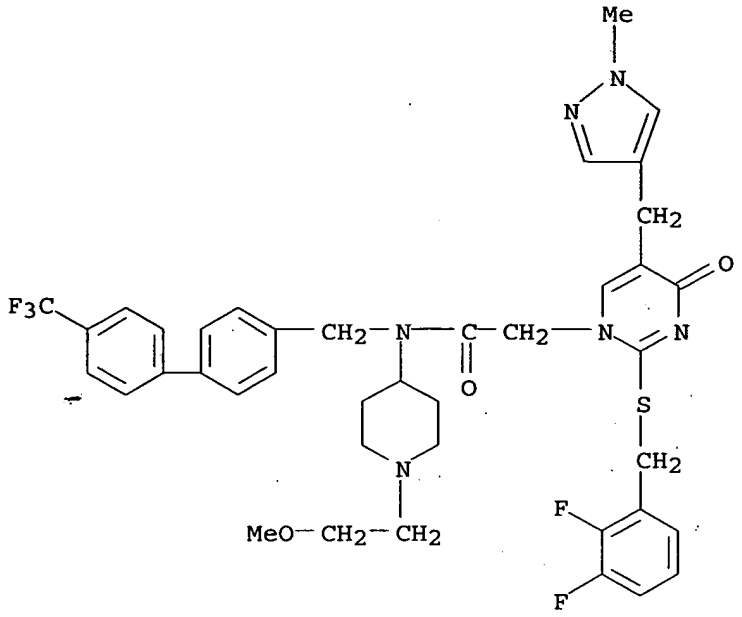
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015786	A1	20030227	WO 2002-EP9068	20020813

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-19793 A 20010814
OTHER SOURCE(S): MARPAT 138:205073
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1, R2 = (un)substituted (hetero)aryl; R3 = Het(alkyl) (wherein Het = (un)substituted 5-7 membered heterocyclyl, bonded directly through a ring carbon atom, comprising N atom and optionally O or S); R4 = (un)substituted (hetero)aryl; R5 = (un)substituted aryl; n = 1-4; X = O, S; Z = CR13R14 (R13, R14 = H, alkyl; or R13 and R14 together with the intervening carbon atom form cycloalkyl)] which are inhibitors of lipoprotein-associated phospholipase A2 (Lp-PLA2) and are of use in therapy, in particular for treating atherosclerosis, were prepared Thus, amidation of N-[1-(2-methoxyethyl)piperidin-4-yl]-4-(4-trifluoromethylphenyl)benzylamine with 1-(carboxymethyl)-2-(2,3-difluorobenzylthio)-5-[(1-methylpyrazol-4-yl)methyl]pyrimidin-4-one (prepns. given) in the presence of HATU and (iso-Pr)2NH in DMF afforded II. The compds. I described in the examples were tested for Lp-PLA2 inhibition and demonstrated IC50 values in the range 1 to 0.01 nM.
IT **500132-05-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2,5-substituted 1-(aminocarbonylalkyl)-pyrimidin-4-ones with Lp-PLA2 inhibitory activity for the treatment of atherosclerosis)
RN 500132-05-8 CAPLUS
CN 1(4H)-Pyrimidineacetamide, 2-[[(2,3-difluorophenyl)methyl]thio]-N-[1-(2-methoxyethyl)-4-piperidinyl]-5-[(1-methyl-1H-pyrazol-4-yl)methyl]-4-oxo-N-[[4'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

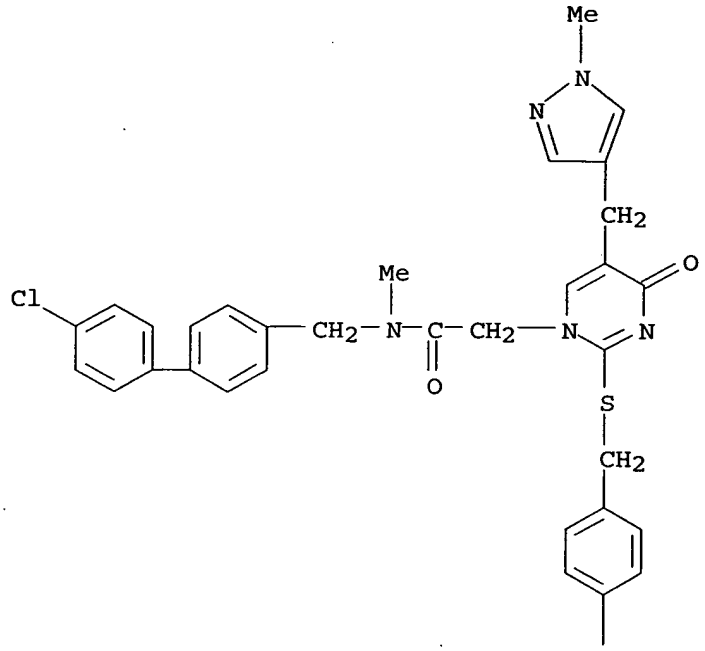
L4 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:641070 CAPLUS
DOCUMENT NUMBER: 138:280725
TITLE: The discovery of SB-435495: A potent, orally active inhibitor of lipoprotein-associated phospholipase A2 for evaluation in man
AUTHOR(S): Blackie, Josie A.; Bloomer, Jackie C.; Brown, Murray J. B.; Cheng, Hung-Yuan; Elliott, Richard L.; Hammond, Beverley; Hickey, Deirdre M. B.; Ife, Robert J.; Leach, Colin A.; Lewis, V. Ann; Macphee, Colin H.; Milliner, Kevin J.; Moores, Kitty E.; Pinto, Ivan L.; Smith, Stephen A.; Stansfield, Ian G.; Stanway, Steven J.; Taylor, Maxine A.; Theobald, Colin J.; Whittaker, Caroline M.
CORPORATE SOURCE: GlaxoSmithKline, Medicines Research Centre, Stevenage, SG1 2NY, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(18), 2603-2606
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The introduction of a functionalized amido substituent into a series of 1-(biphenylmethylacetamido)-pyrimidones has given a series of inhibitors of recombinant lipoprotein-associated phospholipase A2 with sub-nanomolar potency and very encouraging developability properties. Diethylaminoethyl derivative, SB-435495, was selected for progression to man.

IT **304694-18-6P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pyrimidone SB-435495 as a lipoprotein-associated phospholipase A2

inhibitor)
RN 304694-18-6 CAPLUS
CN 1(4H)-Pyrimidineacetamide, N-[(4'-chloro[1,1'-biphenyl]-4-yl)methyl]-2-[[(4-fluorophenyl)methyl]thio]-N-methyl-5-[(1-methyl-1H-pyrazol-4-yl)methyl]-4-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A

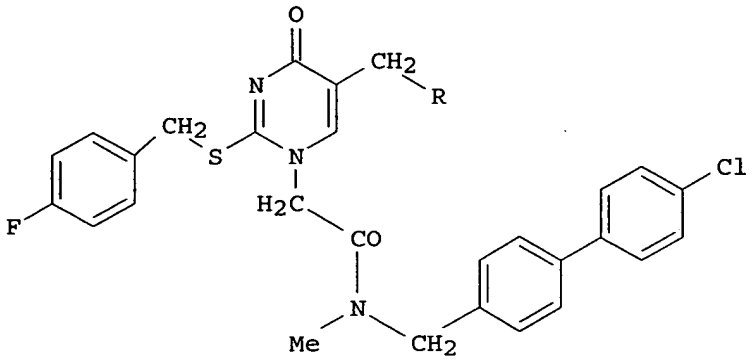


PAGE 2-A

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:900066 CAPLUS
DOCUMENT NUMBER: 136:256730
TITLE: Potent, orally active inhibitors of lipoprotein-associated phospholipase A2: 1-(biphenylmethylamidoalkyl)-pyrimidones
AUTHOR(S): Boyd, Helen F.; Fell, Stephen C. M.; Hickey, Deirdre M. B.; Ife, Robert J.; Leach, Colin A.; MacPhee, Colin H.; Milliner, Kevin J.; Pinto, Ivan L.; Rawlings, D. Anthony; Smith, Stephen A.; Stansfield, Ian G.; Stanway, Steven J.; Theobald, Colin J.; Whittaker, Caroline M.
CORPORATE SOURCE: GlaxoSmithKline, Medicines Research Centre, Stevenage, SG1 2NY, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001),

Volume Date 2002, 12(1), 51-55
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:256730
GI



I

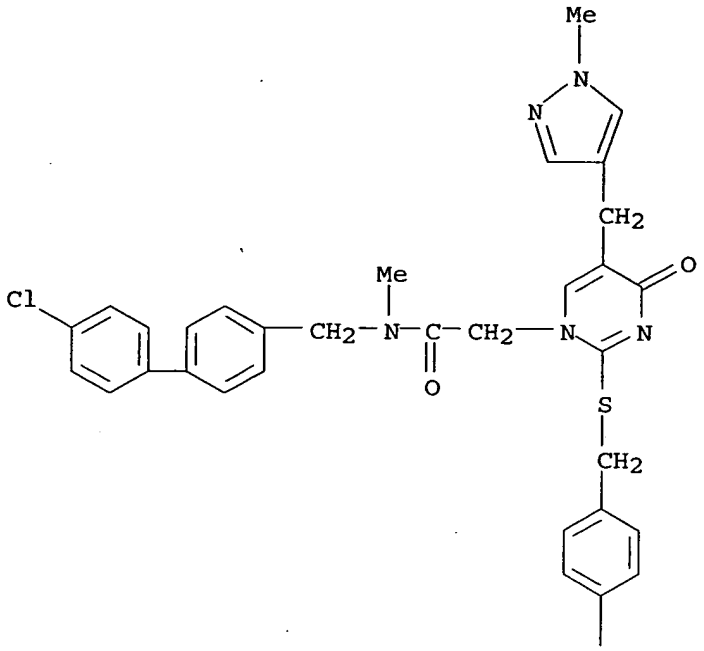
AB A series of 1-(biphenylmethylamidoalkyl)-pyrimidones has been designed as nanomolar inhibitors of recombinant lipoprotein-associated phospholipase A2 with high potency in whole human plasma. Two compds. (I, R=1-methylpyrazol-4-yl or 5-(2-methoxypyrimidin-5-yl)) demonstrated excellent pharmacodynamic profiles which correlated well with their pharmacokinetic effects.

IT **304694-18-6P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(1-(biphenylmethylamidoalkyl)-pyrimidones as inhibitors of lipoprotein-associated phospholipase A2)

RN 304694-18-6 CAPLUS

CN 1(4H)-Pyrimidineacetamide, N-[(4'-chloro[1,1'-biphenyl]-4-yl)methyl]-2-[[(4-fluorophenyl)methyl]thio]-N-methyl-5-[(1-methyl-1H-pyrazol-4-yl)methyl]-4-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A

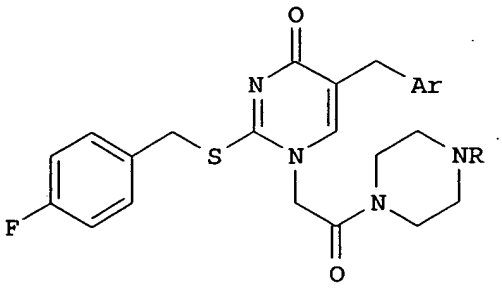


PAGE 2-A

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:518627 CAPLUS
DOCUMENT NUMBER: 135:326949
TITLE: 1-(Arylpiperazinylamidoalkyl)-pyrimidones: orally active inhibitors of lipoprotein-associated phospholipase A2
AUTHOR(S): Bloomer, J. C.; Boyd, H. F.; Hickey, D. M. B.; Ife, R. J.; Leach, C. A.; Macphee, C. H.; Milliner, K. J.; Pinto, I. L.; Rawlings, D. A.; Smith, S. A.; Stansfield, I. G.; Stanway, S. J.; Taylor, M. A.; Theobald, C. J.; Whittaker, C. M.
CORPORATE SOURCE: GlaxoSmithKline, Harlow, Essex, CM19 5AW, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(14), 1925-1929
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

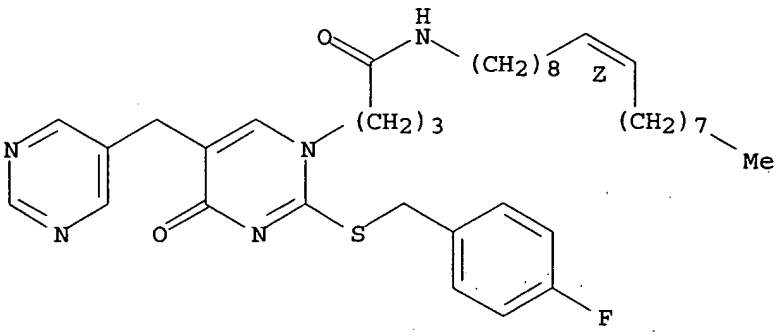
AB The lipophilic 1-substituent in a series of 1-((amido-linked)-alkyl)-pyrimidones, inhibitors of recombinant lipoprotein-associated phospholipase A2, has been modified to give inhibitors of high potency in human plasma and enhanced physicochem. properties. Phenylpiperazineacetamide derivative (I) shows very promising oral activity.

IT **224774-14-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-(arylpiperazinylamidoalkyl)-pyrimidones as orally active inhibitors of lipoprotein-associated phospholipase A2)

RN 224774-14-5 CAPLUS

CN 1(4H)-Pyrimidinebutanamide, 2-[[(4-fluorophenyl)methyl]thio]-N-(9Z)-9-octadecenyl-4-oxo-5-(5-pyrimidinylmethyl)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

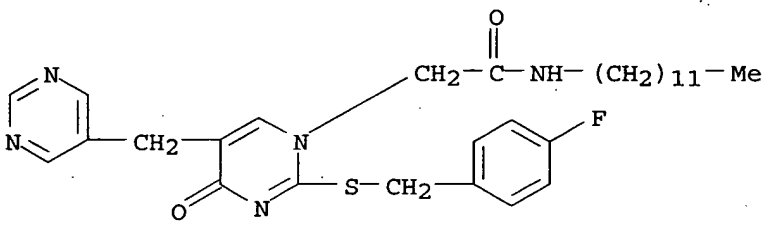
L4 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:177448 CAPLUS
DOCUMENT NUMBER: 135:28649
TITLE: The identification of a potent, water soluble inhibitor of lipoprotein-associated phospholipase A2
AUTHOR(S): Boyd, H. F.; Hammond, B.; Hickey, D. M. B.; Ife, R. J.; Leach, C. A.; Lewis, V. A.; Macphee, C. H.; Milliner, K. J.; Pinto, I. L.; Smith, S. A.; Stansfield, I. G.; Theobald, C. J.; Whittaker, C. M.
CORPORATE SOURCE: New Frontiers Science Park, GlaxoSmithKline

Pharmaceuticals, Harlow, Essex, CM19 5AW, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(5), 701-704
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Modification of the pyrimidone 5-substituent in a series of 1-((amidolinked)-alkyl)pyrimidones, lipophilic inhibitors of lipoprotein-associated phospholipase A2, has given inhibitors of nanomolar potency and improved physicochem. properties. One of the compds. was identified as a potent, highly water soluble, CNS penetrant inhibitor suitable for i.v. administration.

IT **224774-53-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(identification and structure-activity relationships of inhibitors of lipoprotein-associated phospholipase A2)

RN 224774-53-2 CAPLUS
CN 1(4H)-Pyrimidineacetamide, N-dodecyl-2-[[(4-fluorophenyl)methyl]thio]-4-oxo-5-(5-pyrimidinylmethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:844936 CAPLUS
DOCUMENT NUMBER: 134:115922
TITLE: N-1-Substituted pyrimidin-4-ones: novel, orally active inhibitors of lipoprotein-associated phospholipase A2
AUTHOR(S): Boyd, Helen F.; Fell, Stephen C. M.; Flynn, Sean T.; Hickey, Deirdre M. B.; Ife, Robert J.; Leach, Colin A.; Macphee, Colin H.; Milliner, Kevin J.; Moores, Kitty E.; Pinto, Ivan L.; Porter, Rod A.; Rawlings, D. Anthony; Smith, Stephen A.; Stansfield, Ian G.; Tew, David G.; Theobald, Colin J.; Whittaker, Caroline M.
CORPORATE SOURCE: SmithKline Beecham Pharmaceuticals, New Frontiers Science Park, Essex, CM19 5AW, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(22), 2557-2561
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

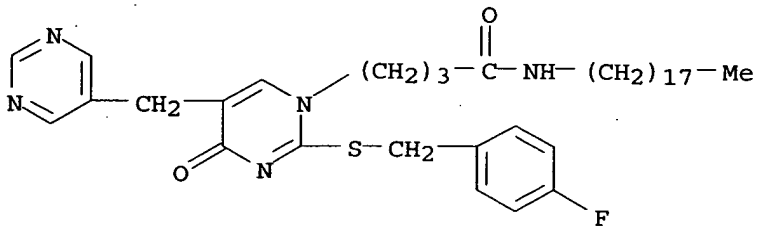
AB From two related series of 2-(alkylthio)pyrimidones, a novel series of 1-[(amidolinked)-alkyl]pyrimidones was designed as nanomolar inhibitors of human lipoprotein-associated phospholipase A2. These compds. show greatly enhanced activity in isolated plasma. Selected derivs. are orally active

with a good duration of action.

IT **224774-13-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(orally active inhibitor of lipoprotein-associated phospholipase A2)

RN 224774-13-4 CAPLUS

CN 1(4H)-Pyrimidinebutanamide, 2-[[(4-fluorophenyl)methyl]thio]-N-octadecyl-4-oxo-5-(5-pyrimidinylmethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:790485 CAPLUS
DOCUMENT NUMBER: 133:335244
TITLE: Preparation of 1-acetamido-2-(arylalkylthio)-4-pyrimidinones as lipoprotein associated phospholipase A2 inhibitors
INVENTOR(S): Fenwick, Ashley Edward; Hickey, Deirdre Mary Bernadette; Ife, Robert John; Leach, Colin Andrew; Pinto, Ivan Leo; Smith, Stephen Allan
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066567	A1	20001109	WO 2000-EP3727	20000425
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2371671	AA	20001109	CA 2000-2371671	20000425
EP 1175408	A1	20020130	EP 2000-920741	20000425
EP 1175408	B1	20041201		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200103216	T2	20020422	TR 2001-200103216	20000425
BR 2000010220	A	20020514	BR 2000-10220	20000425

JP 2002543190	T2	20021217	JP 2000-615598	20000425
AU 766003	B2	20031009	AU 2000-41203	20000425
NZ 515137	A	20031031	NZ 2000-515137	20000425
EP 1479671	A1	20041124	EP 2004-77397	20000425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, CY				
AT 283845	E	20041215	AT 2000-920741	20000425
PT 1175408	T	20050429	PT 2000-920741	20000425
ES 2233361	T3	20050616	ES 2000-920741	20000425
NO 2001005329	A	20011031	NO 2001-5329	20011031
ZA 2001008991	A	20021020	ZA 2001-8991	20011031
US 6953803	B1	20051011	US 2002-30661	20020422
HK 1044757	A1	20050708	HK 2002-104602	20020620
US 2004167142	A1	20040826	US 2004-776876	20040211

PRIORITY APPLN. INFO.: GB 1999-10048 A 19990501
GB 2000-2096 A 20000128
EP 2000-920741 A3 20000425
WO 2000-EP3727 W 20000425
US 2002-30661 A3 20020422

OTHER SOURCE(S): MARPAT 133:335244

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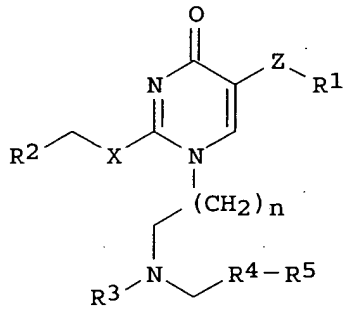

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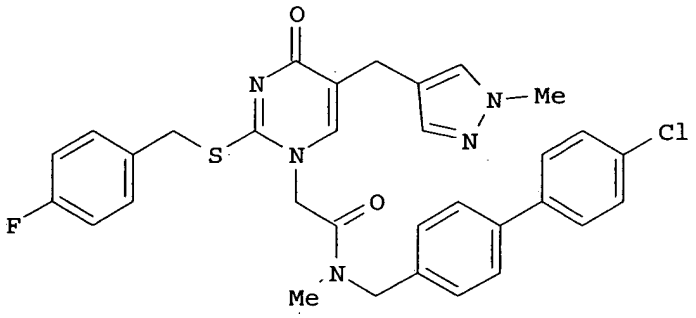


II

AB The title compds. (I) [wherein R1, R2, and R4 = independently (un)substituted (hetero)aryl; R3 = H or (un)substituted alkyl; R5 = (un)substituted aryl; n = 1-4, preferably 1 or 3; X = O or S; Z = CR13R14; R13 and R14 = independently H or alkyl; or CR13R14 = cycloalkyl] were prepared as inhibitors of the phospholipase A2 enzyme Lp-PLA2 for the treatment of atherosclerosis. For example, II was formed by amidation of 1-(carboxymethyl)-2-(4-fluorobenzylthio)-5-((1-methylpyrazol-4-yl)methyl)pyrimidin-4-one with N-methyl-4-(4-chlorophenyl)benzylamine

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

(preparation for both starting materials given). I inhibited recombinant Lp-PLA2 enzyme activity with IC50 values in the range of 0.001 to 0.00005 μM.

IT **304694-35-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of 1-acetamido-2-(arylalkylthio)-4-pyrimidinone Lp-PLA2 inhibitors by amidation of 1-(carboxymethyl)-2-(arylalkylthio)-4-pyrimidinones with (hetero)arylalkylamines for the treatment of atherosclerosis)

RN 304694-35-7 CAPLUS

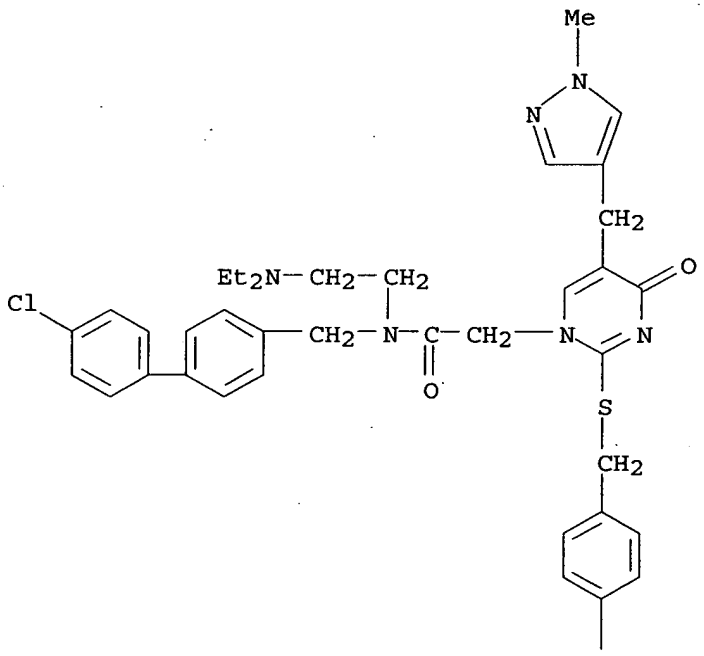
CN 1(4H)-Pyrimidineacetamide, N-[(4'-chloro[1,1'-biphenyl]-4-yl)methyl]-N-[2-(diethylamino)ethyl]-2-[[(4-fluorophenyl)methyl]thio]-5-[(1-methyl-1H-pyrazol-4-yl)methyl]-4-oxo-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 304694-31-3

CMF C37 H40 Cl F N6 O2 S

PAGE 1-A

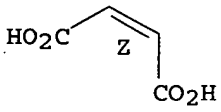


PAGE 2-A

CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:144863 CAPLUS
DOCUMENT NUMBER: 132:180594
TITLE: Preparation of pyrimidinone derivatives for the treatment of atherosclerosis
INVENTOR(S): Leach, Colin Andrew; Smith, Stephen Allan
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000010980	A1	20000302	WO 1999-EP6093		19990818
W: CA, JP, US					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
EP 1105377	A1	20010613	EP 1999-942894		19990818
EP 1105377	B1	20031008			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002523402	T2	20020730	JP 2000-566254		19990818
AT 251613	E	20031015	AT 1999-942894		19990818
US 6559155	B1	20030506	US 2001-763492		20010221
PRIORITY APPLN. INFO.:			GB 1998-18375	A	19980821
			GB 1999-2009	A	19990129
			WO 1999-EP6093	W	19990818

OTHER SOURCE(S): MARPAT 132:180594
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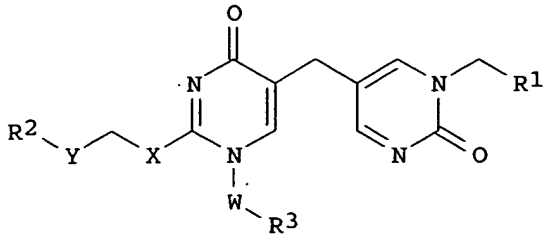

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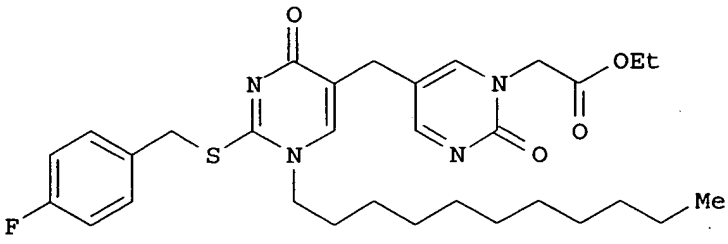


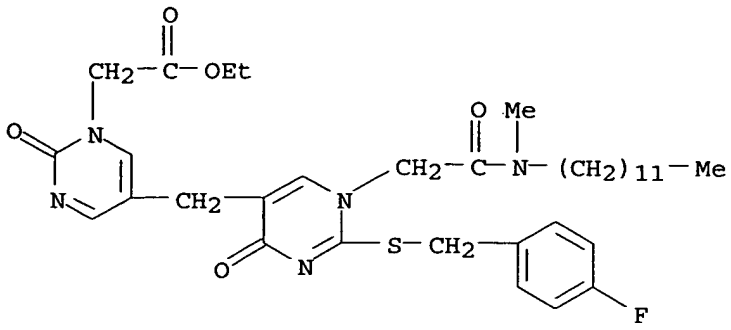
II

AB The title compds. [I; R1 = CO2H, salt thereof, CO2R10, etc.; R2 = mono- or bicyclic aromatic ring system, mono- or bicyclic heteroarom. ring system; R3 = alkyl, cycloalkyl, cycloalkylalkyl, etc.; W = SO2, a bond; X = O, S; Y = A1-A2-A3 (wherein A1 and A3 = a bond, alkylene; A2 = a bond, O, S, etc.; providing that when A2 = O, S, SO, SO2 or CONH, A3 contains at least two carbon atoms linking the A2 group and the CH2 group); R10 = alkyl, pharmaceutically acceptable in vivo hydrolysable ester] which are inhibitors of the enzyme LpPLA2, and are useful in treating inter alia atherosclerosis, were prepared E.g., a 3-step synthesis of pyrimidinone II starting with 1-undecyl-5-(2-methoxypyrimidin-5-ylmethyl)-2-thiouracil, was given. Compds. I were tested for Lp-PLA2 inhibition and showed IC50 of 0.0004-3.2 μM.

IT **259532-13-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyrimidinones as antiatherosclerotics)

RN 259532-13-3 CAPLUS

CN 1(2H)-Pyrimidineacetic acid, 5-[[1-[2-(dodecylmethylamino)-2-oxoethyl]-2-[[(4-fluorophenyl)methyl]thio]-1,4-dihydro-4-oxo-5-pyrimidinyl]methyl]-2-oxo-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

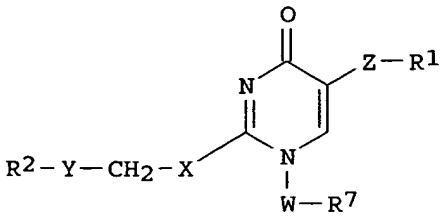
L4 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:325924 CAPLUS
DOCUMENT NUMBER: 130:352278
TITLE: Preparation of pyrimidinone derivatives as Lp-PLA2 inhibitors
INVENTOR(S): Hickey, Deirdre Mary Bernadette; Ife, Robert John; Leach, Colin Andrew; Pinto, Ivan Leo; Porter, Roderick Alan; Smith, Stephen Allan
PATENT ASSIGNEE(S): Smithkline Beecham PLC, UK
SOURCE: PCT Int. Appl., 210 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9924420	A1	19990520	WO 1998-EP6988		19981023
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2309177	AA	19990520	CA 1998-2309177		19981023
AU 9911575	A1	19990531	AU 1999-11575		19981023
EP 1028955	A1	20000823	EP 1998-954482		19981023
EP 1028955	B1	20030716			
R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SI					
JP 2001522844	T2	20011120	JP 2000-520434		19981023
ES 2203988	T3	20040416	ES 1998-954482		19981023
ZA 9810112	A	20000505	ZA 1998-10112		19981105
US 6417192	B1	20020709	US 2000-530713		20000628
US 2002120139	A1	20020829	US 2002-115452		20020402
PRIORITY APPLN. INFO.:			GB 1997-23352	A	19971106
			GB 1997-23358	A	19971106
			WO 1998-EP6988	W	19981023
			US 2000-530713	A3	20000628

OTHER SOURCE(S): MARPAT 130:352278

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

GI



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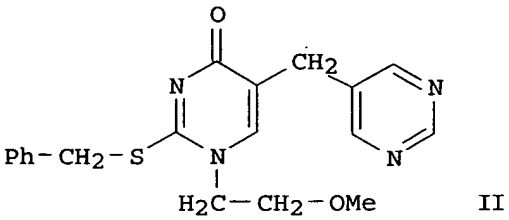


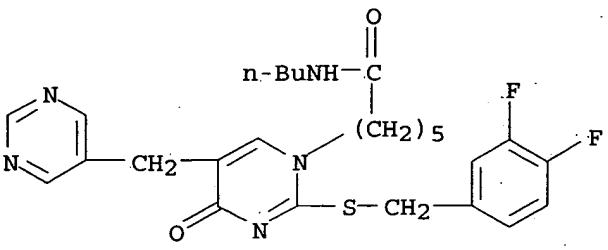
II

AB The title compds. I [Z is a bond and R1 is halo, or Z is CR3R4 wherein R3 and R4 are each hydrogen, alkyl, or CR3R4 = cycloalkyl ring; R1 is aryl or heteroaryl group optionally substituted by 1 - 4 substituents; X = O, S; Y is A1A2A3 in which A1 and A3 each represent a bond or alkylene, and A2 represents a bond or O, S, etc.; a proviso is given; R2 is aryl or heteroaryl group optionally substituted by 1 - 4 substituents; W is a bond and R7 is hydrogen; or W is SO2 or a bond; R7 is R1 or hydrocarbyl group (further detail on said hydrocarbyl group is given)] are prepared I are useful in the treatment of atherosclerosis (no data). For example, pyrimidinone derivative II was prepared Compds. of this invention were found to have IC50 values in the range 0.0001 to 60 μM in the test for lipoprotein-associated phospholipase A2 (Lp-PLA2) inhibition.

IT **224778-23-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and therapeutic effect of pyrimidinone derivs. as Lp-PLA2 inhibitors)

RN 224778-23-8 CAPLUS

CN 1(4H)-Pyrimidinehexanamide, N-butyl-2-[[(3,4-difluorophenyl)methyl]thio]-4-oxo-5-(5-pyrimidinylmethyl)- (9CI) (CA INDEX NAME)



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RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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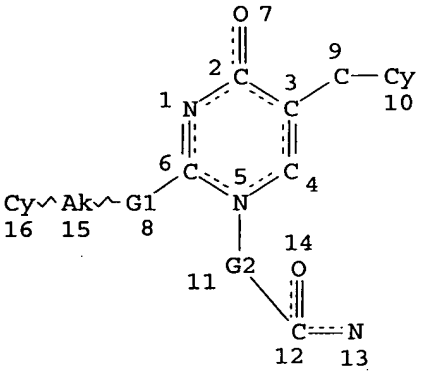


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CA SUBSCRIBER PRICE                               -8.03      -8.03


Prepared by: Mary Hale @2-2507 Rem Bldg 1D86
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   19 DEC 2005  HIGHEST RN 870234-75-6
DICTIONARY FILE UPDATES:  19 DEC 2005  HIGHEST RN 870234-75-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

*********************************************************************
*                                                                   *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                   *
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Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> s benzyl(l)aminocarbonylmethyl(l)pyrimidin?
        280779 BENZYL
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FILE COVERS 1907 - 20 Dec 2005 VOL 143 ISS 26
FILE LAST UPDATED: 19 Dec 2005 (20051219/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

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L7          1 L6 OR BENZYL(L)AMINOCARBONYLMETHYL(L)PYRIMIDIN?
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=> d ibib abs hitstr

L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:790484 CAPLUS
DOCUMENT NUMBER: 133:350250
TITLE: Preparation of 1-(piperazinylcarbonylalkyl)-2-(arylalkylthio)-4-pyrimidinones as lipoprotein associated phospholipase A2 inhibitors
INVENTOR(S): Hickey, Deirdre Mary Bernadette; Ife, Robert John; Leach, Colin Andrew; Smith, Stephen Allan
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066566	A1	20001109	WO 2000-EP3726	20000425
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Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

EP 1173424 A1 20020123 EP 2000-927053 20000425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2002543189 T2 20021217 JP 2000-615597 20000425
PRIORITY APPLN. INFO.: GB 1999-10079 A 19990501
WO 2000-EP3726 W 20000425
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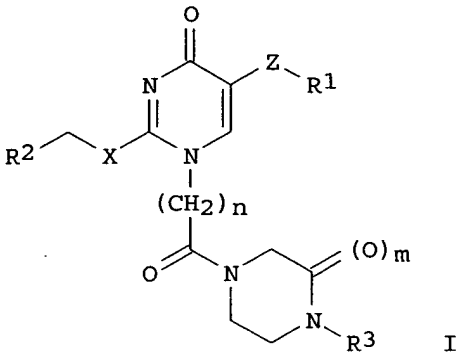

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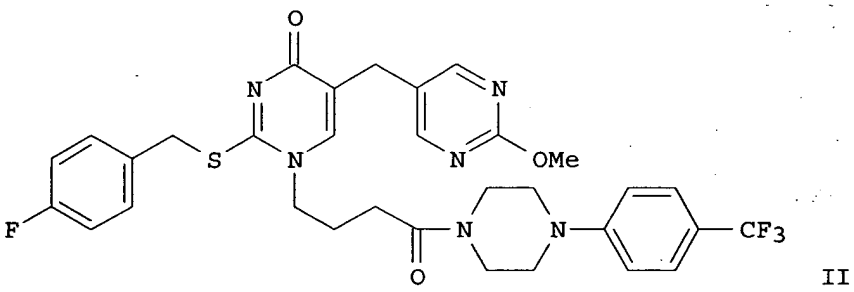


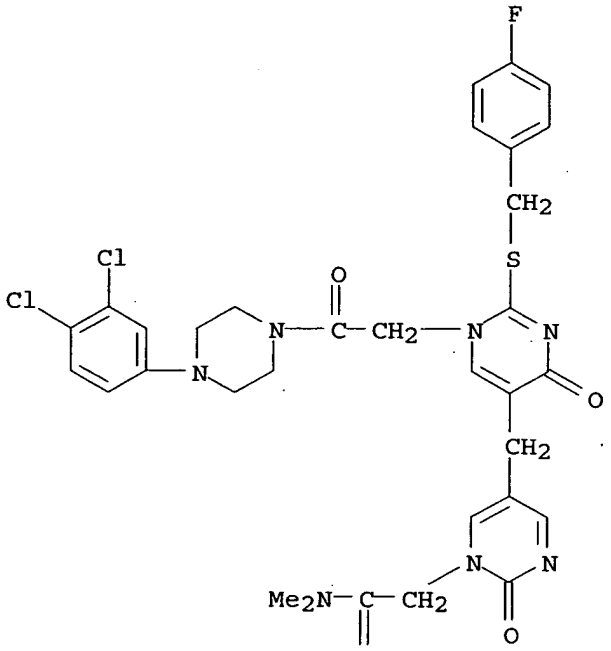
II

AB The title compds. (I) [wherein R1 and R2 = independently (un)substituted (hetero)aryl; R3 = H, alkyl, alkenyl, (un)substituted (hetero)arylalkyl, alkylcarbamoyl, alkylsulfamoyl, alkylsulfonyl, or acyl; m = 0 or 1; n = 1-4, preferably 1 or 3; X = O or S; Z = CR13R14; R13 and R14 = independently H or alkyl; or CR13R14 = cycloalkyl] were prepared as inhibitors of the phospholipase A2 enzyme Lp-PLA2 for the treatment of atherosclerosis. For example, II was formed by amidation of 1-(3-carboxyprop-1-yl)-2-(4-fluorobenzylthio)-5-(2-methoxypyrimid-5-ylmethyl)pyrimidin-4-one (preparation given) with 1-(4-trifluoromethylphenyl)piperazine. II inhibited recombinant Lp-PLA2 enzyme activity with an IC50 of 2 nM.

IT **304903-61-5P**, 1-[4-(3,4-Dichlorophenyl)piperazin-1-ylcarbonylmethyl]-2-((4-fluorobenzyl)thio)-5-[1-(dimethylaminocarbonylmethyl)-2-oxopyrimid-5-ylmethyl]pyrimidin-4-one
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1-(piperazinylcarbonylalkyl)-2-(arylalkylthio)-4-pyrimidinone Lp-PLA2 inhibitors by amidation of 1-(carboxyalkyl)-2-(arylalkylthio)-4-pyrimidinones with piperazines)

RN 304903-61-5 CAPLUS
CN 1(2H)-Pyrimidineacetamide, 5-[[1-[2-[4-(3,4-dichlorophenyl)-1-piperazinyl]-2-oxoethyl]-2-[[(4-fluorophenyl)methyl]thio]-1,4-dihydro-4-oxo-5-pyrimidinyl]methyl]-N,N-dimethyl-2-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L3 191 S L1 FUL

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FILE 'REGISTRY' ENTERED AT 13:29:07 ON 20 DEC 2005
L6 1 S BENZYL(L)AMINOCARBONYLMETHYL(L)PYRIMIDIN?

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

FILE 'CAPLUS' ENTERED AT 13:29:47 ON 20 DEC 2005
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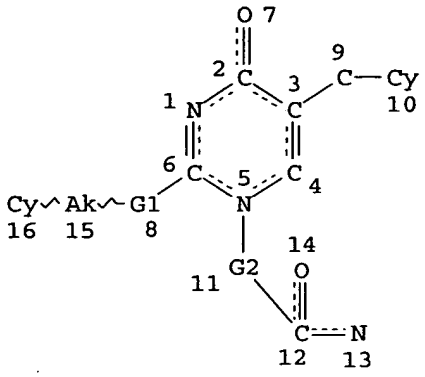

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STEREO ATTRIBUTES: NONE
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